DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

m2681n

MAY 28 1999

WARNING LETTER

VIA FEDERAL EXPRESS
VIA FACSIMILE

Mr. Nigel L.C. Broggio
Managing Director and Chairman
Medical Wire & Equipment Co. (Bath) Ltd.
Potley Road
Corsham, Wiltshire, England UK SN13 9RT

Dear Mr. Broggio:

During an inspection of your firm located at Corsham, Wilshire, England on March 31 and April 1, 1999, our Investigator determined that your firm manufactures microbiological specimen collection and transport devices, such as Transtubes and Transwabs. We have reviewed your response to the FDA 483 received on May 3, 1999. The transport medium products are devices as defined by section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). The above stated inspection revealed that these devices are adulterated under section 501(h) of the Act, in that the methods used in, or the facilities or controls used in the manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulations for Medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to investigate the cause of nonconformities relating to product, processes, and the quality system, as required by 21 CFR 820.100(a)(2). For example, sterility testing of [redacted] Retesting found [redacted] The batch was released on the basis that all other results met specifications. No investigation was done to determine how [redacted] during testing. Furthermore, there is no data showing that this is a typical sterility testing false positive rate. [redacted] was also released on a similar basis even though [redacted] (FDA 483 item 8)

YOUR RESPONSE

1. Not Adequate. Your investigation is not clear on the cause of the contamination. The investigation is not adequate to demonstrate that the product is not the cause of the failure. You do not address previously shipped lots.

2. Failure to control in-process acceptance activities to ensure that specified requirements for in-process product are met, as required by 21 CFR 820.80(c). For example:

A. In-process Transwab bacteria collection and transport device testing requirements are not always met. For example, the requirement to contact the Production Manager if more [redacted] consecutive plate is found with [redacted] is not being followed. The requirement to irradiate at [redacted] samples containing [redacted] is not verified. (FDA 483 item 1)

B. The in-process medium test procedure allows retesting of samples and acceptance of a batch even [redacted] is confirmed as having survived irradiation. (FDA 483 item 2)

YOUR RESPONSE

2A. Not Adequate. The procedure has been changed, however no reference was made concerning lots produced following the previous procedure.

2B. Not Adequate. The procedure was changed to reference the disposal of the batch if Gram positive rods survived after radiation, however it did not reference disposal of the batch for survival of other organisms.

3. Failure to ensure that the device history records are maintained to demonstrate that the device is manufactured in accordance with the device master record, as required by 21 CFR 820.184. For example, incubation starting and ending (reading) times and temperatures for spore swab sterility samples, sterility samples, in-process Gram positive rod evaluation samples, and performance testing with test organisms, are not recorded. (FDA 483 item 13)

YOUR RESPONSE

3. Adequate. A new testing form was provided that includes starting and ending reading times for sterility samples.

4. Failure to ensure that all devices conform to their specifications where environmental conditions could reasonably be expected to have an adverse effect on product quality, as required by 21 CFR 820.70(c). For example, the [redacted] sterilization dose audits are not adequate because the bioburden levels are not determined as part of the quarterly dose audits. (FDA 483 item 3e)

YOUR RESPONSE

4. Not Adequate. You are reviewing the dose auditing and have promised a response.

5. Failure to control and monitor production processes to ensure that a device conforms to its specification, as required by 21 CFR 820.70(a)(2). For example:

A. The audit done in July 1997 found [redacted] samples not sterile. Repeat testing was done using [redacted] samples from another lot. No justification is provided for invalidating the initial test results. (FDA 483 item 3a)

B. The audit done in September 1997 found [redacted] samples not sterile. Repeat testing was done using [redacted] samples. [redacted] samples were found non-sterile. There is no justification for invalidating the initial results and no basis for accepting the results from the second audit [redacted] samples are allowed to be non-sterile). (FDA 483 item 3b)

C. The audit done in December 1997 used a verification dose of [redacted] The sterilization dose lower limit is based on a verification dose of [redacted] (FDA 483 item 3c)

D. The audit done in March 1999 used a verification dose of [redacted] (FDA 483 item 3d)

YOUR RESPONSE

5A/D. Not Adequate. You are reviewing the dose auditing and have promised a response after the week of 5/24/99.

6. Failure to verify by subsequent inspection and test, that the process is validated with a high degree of assurance and approved according to established procedures as required by 21 CFR 820.75(a). For example, microbiological test methods have not been validated to

confirm that organisms of interest, such as [redacted] can be recovered. (FDA 483 item 14)

YOUR RESPONSE

6. Not Adequate. No validation of the microbiological test methods was provided.

7. Failure to control production processes to ensure that a device conforms to its specifications as required by 21 CFR 820.70(a). For example:

A. No precision specifications have been established for inter-lot and intra-lot reference organism recoveries for the Transwab device. For example 1) [redacted] test organism used for batches [redacted] performance testing had [redacted] samples, respectively, recover at a level of [redacted]. Typical recoveries are at [redacted] levels (dense growth/dense confluent growth); 2) Testing of batch [redacted] using the [redacted] test organism found the following varying recoveries for the [redacted] performance test samples: [redacted] (FDA 483 item 5)

B. The contract sterilizer has imposed an upper limit sterilization dose of [redacted]. However, the Medical Wire & Equipment upper limit is set at [redacted] No statistical assessment has been done to confirm that the use and testing of dosimeters by MW&E will insure that any product dosed at levels exceeding [redacted] will be identified. (FDA 483 item 9)

YOUR RESPONSE

7A. Not Adequate. You provided copies of performance testing for three lots that appeared to be consistent. They did not address specifications for inter-lot and intra-lot reference organism recoveries for the Transwab device.

7B. Adequate. The procedure was changed to require the contract sterilizer to report any lots dosed above 18 kGy. The high dose lots will be sampled and monitored.

8. Failure to include production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications in the device master record, as required by 21 CFR 820.181(b). For example, the

specifications of the cartons used for packaging transport media prior to radiation sterilization are not included in the device master record. (FDA 483 item 11)

YOUR RESPONSE

8. Adequate. A copy of the specifications for the cartons has been included in the master record has been provided.

9. Failure to document calibration records for inspection, measuring, and test equipment as required by 21 CFR 820.72(a). For example, the micrometer readings obtained before calibration are not recorded. (FDA 483 item 15)

YOUR RESPONSE

9. Not Adequate. Your response did not address keeping records of the micrometer reading before calibration to determine if the product was in specification.

The Transwab and Transtube devices are misbranded under section 502(f)(1) of the Act in that their labeling bears claimed expiration dates which are false or misleading in that such expiration dating is not based on a written stability testing program, or based on valid test results. As required by 21 CFR 809.10, such information shall be determined by reliable, meaningful, and specific test methods, such as those described in 21 CFR 211.166.

Please advise us on your plans for product that was manufactured under the above violative conditions and shipped to the U.S.

This letter is not intended to be an all-inclusive list of deficiencies at your Corsham, Wiltshire, England facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by FDA. If the causes are determined to be systems problems you must promptly initiate permanent corrective actions.

Given the serious nature of these violations of the Act, all devices manufactured by Medical Wire & Equipment Co. (Bath) Ltd., Corsham, Wiltshire, England may be detained upon entry into the U.S.until these violations have been corrected.

In order to remove the devices from this detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections have been verified, your products may resume entry into this country.

Please notify this office in writing as to the specific steps you have taken, or intended to take, to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. We acknowledge the receipt of your response to the FDA 483 received on May 3, 1999. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. Please address your response and any questions to:

Mr. Robert G. Brett, CSO
U.S. Food and Drug Administration
Office of Compliance (HFZ-321)
Division of Enforcement 1
In Vitro Diagnostic Devices Branch
2098 Gaither Road
Rockville, Maryland 20850
U.S.A.

Should you require any assistance in understanding the contents of this letter, do not hesitate to contact Mr. Brett at the above address or at (301) 594-4588 or FAX (301) 594-4636.

Sincerely yours,

Adrianne Galdi

for Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health